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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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STAAS & HALSEY LLP SUITE 700 1201 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			EXAMINER SKOWRONEK, KARL HEINZ R	
			ART UNIT	PAPER NUMBER
			1631	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/571,669

Applicant(s)

SCHUERMANN ET AL.

Examiner

KARLHEINZ R. SKOWRONEK

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2006.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-14 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 6-14 is/are rejected.
7) ☒ Claim(s) 6 and 14 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 13 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Claim Status

Claims 6-14 are pending.

Claims 1-5 are cancelled.

Claims 6-14 have been examined.

Claims 6-14 are rejected.

Claims 6 and 14 are objected to.

Priority

This application has the filing date of 13 March 2006 and is the National Stage filing under 35 USC371 of International application PCT/EP04/51835 which was filed on 18 August 2004 and claims priority of German Patent Application 103 42 274.9 which was filed on 12 September 2003.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

No information disclosure statements have been filed.

Drawings

The drawings filed on 13 March 2006 are acceptable.

Claim Objections

Claims 6 and 14 are objected to because of the following informalities: Claim 6 recites "a plurality of gene expression pattern" in line 3, where the term "pattern" should

be plural; Claim 6 recites "a regulatory network of genome and proteome" in line 8, which is grammatically inaccurate; Claim 6 recites "strengthening" in line 17, but should recite "strengthened" for grammatical reasons; Claim 6 recites "inhibiting" in line 17, but should recite "inhibited" for grammatical reasons; Claim 14 recites "a regulatory network of genome and proteome" in line 7-8, which is grammatically inaccurate; Claim 14 recites "strengthening" in line 16, but should recite "strengthened" for grammatical reasons; and Claim 14 recites "inhibiting" in line 16, but should recite "inhibited" for grammatical reasons. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 6-13 are directed to a process in which gene expression patterns are inputs to a neuronal network to create a dynamic model of gene regulation in a genome. The following analysis is taken from the guidance provided in the MPEP at 2104.IV, "Determine Whether the Claimed Invention Complies with 35 USC101". The claims are directed to processes. Here the claims are directed to the abstract idea of a mathematical, dynamic model of gene regulation from gene expression patterns using a neuronal network model. The processes do not recite a physical transformation of matter from one state to another. Giving the claims the broadest reasonable interpretation, the claims read on mental steps. In *Comiskey (In re Comiskey*, 84 USPQ2d 1670) the court established that "the application of human

intelligence to the solution of practical problems is not and of itself patentable" (at 1680). In *Comiskey*, the court stated explicitly "mental processes - or processes of human thinking - standing alone are not patentable even if they have a practical application" (at 1679). The court in *Comiskey* stated, "Following the lead of the Supreme Court, this court and our predecessor court have refused to find processes patentable when they merely claimed a mental process standing alone and untied to another category of statutory subject matter even when a practical application was claimed" (at 1680). The court's recent decision in *In re Bilski* confirmed, "a process is patent-eligible under 35 USC 101 if it is tied to a particular machine or apparatus or if it transforms a particular article into a different state or thing" (*In re Bilski*, 88 USPQ at 1391, 2008). In the instant claims, the process is not tied to a class of statutory invention. Output is insignificant post-solution activity and does not represent a significant tie to another category of invention. The court in *Comiskey*, stated "the court rejected the notion that mere recitation of a practical application of an abstract idea makes it patentable, concluding that '[a] competent draftsman could attach some form of post-solution activity to almost any mathematical formula'" citing *Flook* (437 U.S. at 586, 590). The recent decision in *Bilski* confirmed the court's position regarding insignificant pre- or post-solution activity (i.e. insignificant extra-solution activity) as stated in *Comiskey* (see *In re Bilski*, 88 USPQ2d 1385 (Fed. Cir. 2008) at p. 13-96-1397). Applicant is encouraged to consider the recent BPAI informative decisions *Exparte Langemyr* (No. 2008-1495 (28 May 2008)) and *Exparte Biliski* (No. 2002-2257 (26 September 2006)) for further clarification of the above grounds of rejection.

Claim Rejections - 35 USC § 112

Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is unclear with respect to the "a cell" as recite in line 5. The metes and bounds are indefinite because it is unclear which cell of the similar cells used in obtaining the plurality of gene expression patterns is used to determine the rate of gene expression. Claims 7-13 are also rejected because they depend from claim 6, and thus contain the above issues due to said dependence.

Claim 6 is unclear with respect to the "a gene" in line 10. The metes and bounds of the claim are rendered indefinite because a plurality of genes are considered in line 3 and the recitation a gene in line 10 does not provide a measure of which gene of the plurality is represented by the "a neuron" of line 11.

Claim 6 is further unclear with respect to the recitation of "a first" and "a second gene" in lines 14-16. The metes and bounds of the claim are rendered indefinite because only a single gene is represented in the neuronal network making it unclear which if any of the "a first" or "a second" genes are the gene recited in line 10.

Claim 6 is indefinite with respect to the recitation of "a neuron" as in lines 15-16. The mete and bounds of the claim are rendered indefinite because the recitation of "a

neuron" makes it unclear what relation the neurons of lines 15-16 have to the single neuron that forms the neural network in line 10-13.

Claim 6 is unclear with respect to the recitation of "a cell" in line 8-9. The metes and bounds of the claim are rendered indefinite by the term "a cell" in line 8-9 because the recitation of the term makes it unclear if the same cell as is used to determine the expression rate, is used to form the dynamic model.

Claim 7 is unclear with respect to the recitation of "a first neuron" and "a second neuron" in line 3. The metes and bounds of the claim are rendered indefinite because the claim provides no measure to determine if the first and second neurons as recited in line 3 are the same as the neurons of claim 6, line 15-16 or if they are different. The claim is made further unclear because the neuronal network is formed by a single neuron however at least 5 neurons are recited (3 in claim 1 and 2 in claim 7).

Claims 9, 11, 12, and 13 are indefinite because they are directed to the use of the gene expression patterns to reduce a level of networking without reciting active steps. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 14 is unclear with respect to the "a gene" in line 9. The metes and bounds of the claim are rendered indefinite because a plurality of genes are considered in line 3 and the recitation a gene in line 9 does not provide a measure of which gene of the plurality is represented by the "a neuron" of line 11.

Claim 14 is further unclear with respect to the recitation of "a first" and "a second gene" in lines 13-15. The metes and bounds of the claim are rendered indefinite

because only a single gene is represented in the neuronal network making it unclear which if any of the "a first" or "a second" genes are the gene recited in line 9.

Claim 14 is indefinite with respect to the recitation of "a neuron" as in lines 14-15. The metes and bounds of the claim are rendered indefinite because the recitation of "a neuron" makes it unclear what relation the neurons of lines 14-15 have to the single neuron that forms the neural network in line 9-12.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lukashin (WO 2001/034789), and in view of Vohradsky (FASEB J., Vol. 15, p. 846-854, 2001).

The claims are directed to a method comprising determining a plurality of gene expression patterns for genes of a cell, determining the gene expression rate of the genes and at least partially reconstructing a chronological sequence for the gene expression patterns; forming a dynamic model of a regulatory network representing the genome and proteome of the cell deduced from a neuronal network.

The limitations of claims 7-13 are product by process limitations of the neural network. Claims 6-13 are obvious over Lukashin alone who shows a method and system that can be used to identify pharmaceutical targets using gene expression patterns in a chronological sequence from which a dynamic model of a genomic regulatory network formed with a neural network. However in the interest of compact prosecution the product-by-process limitations of the claims have also been treated.

Lukashin shows a method and system that comprises determining a plurality of gene expression patterns for genes of a cell (p. 8, lines 17-23). Lukashin shows the determination of a time depend value, V_T , the activity of a neuron represented by gene expression level, which reads on the steps of determining a rate of expression and representing the rate of expression as an activity of a neuron (p. 6, line 15-19).

Lukashin shows at least partially reconstructing a chronological sequence for the gene expression patterns (p. 8, line 17-19). Lukashin shows forming a dynamic model of a regulatory network representing the genome and proteome of the cell deduced from a neuronal network (p. 8, line 11-12). Lukashin shows each gene is represented by a neuron (p. 6, line 15). Lukashin shows a regulatory effect is represented using a synaptic connection and the connection changes signs: positive for strengthening and negative for inhibiting (p. 6, line 19-22). Lukashin shows the embodiments of claims 9 and 11-13, in which the neuronal network is adapted to each specific gene profile so as to reduce the level of networking. With respect to this limitation, Lukashin shows genes expression patterns were concatenated and cluster based on similarities between temporal behaviors of the gene (p. 8, line 20-26). Lukashin shows doing this reduce the level of networking (p. 13, line 23-30). Lukashin suggest information related to novel connections between clusters can then be used to model the interactions between the genes of the identified clusters having novel connections.

Lukashin does not show the representation of a regulatory effect by weighting a connection.

Vohradsky shows a neural network model of gene expression from which a genomic and proteomic regulatory network is deduced. Vohradsky shows that regulatory effects are represented by weighting the synaptic connection (p. 847, col. 2). Vohradsky shows each gene of a gene expression pattern is represented by a node, or neuron, in the network (figure 1). Vohradsky shows the expression rate of a gene is determined to be the level of gene expression at a time and is represented as an

instantaneous rate in equation 4 (p. 847). Vohradsky shows each node represents both the gene and the gene's product, or encoded protein (p. 849, col.2). Regarding claim 7, Vohradsky shows post translation modifications are represented by a synaptic connection with a multiplicative term (p. 849, col. 2). Regarding claim 8, Vohradsky shows that an external input is represented by an input node (p. 847, col. 2). Vohradsky shows the advantage of the model presented in this paper is that it is continuous in time, does not use artificial elements, and uses a transfer function that transforms the input to a shape close to the one observed in natural processes (p. 852, col. 2).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the method and systems of Lukashin for inferring a regulatory network using a neural network and gene expression data with the neural network model and deduced regulatory network of Vohradsky because Vohradsky shows the model has the advantages of being continuous in time, does not use artificial elements, and the transfer function transforms the input to a shape close to the one observed in natural processes. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method and systems of Lukashin for inferring a regulatory network using a neural network and gene expression data with the neural network model and deduced regulatory network of Vohradsky because the substitution of one known element for another would have yielded predictable results.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone

number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/
Examiner, Art Unit 1631

13 May 2009